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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/874,103 | 06/05/2001 | Herman F. Staats | 180/102/2 | 6817 |

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| EXAMINER | |
|---|---|
| LANDSMAN, ROBERT S | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | |

DATE MAILED: 03/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/874,103 | STAATS ET AL. | |
| | Examiner | Art Unit | |
| | Robert Landsman | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *64-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *1. Formal Matters*

A. The Amendment dated 12/22/03 has been entered into the record.

B. Claims 64-84 are pending in the application and are the subject of this Office Action.

C. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

### *2. Double Patenting*

A. The rejection of claims 64-84 under the judicially created doctrine of obviousness-type double patenting has been withdrawn since Applicants have filed a Terminal Disclaimer over U.S. Patent 6,270,758.

### *3. Claim Rejections - 35 USC § 112, second paragraph*

A. The rejection of claims 64-84 under 35 USC 112, second paragraph, has been withdrawn in view of Applicants' arguments that the issue of whether or not the composition is water soluble or insoluble does not render the claims indefinite. Furthermore, Applicants argue that water-insoluble antigen-adjuvant compositions are well-known in the art.

### *4. Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 64-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al. (reference C21 on the IDS dated 8/20/03) in view of Elson et al. (reference C5 on the IDS dated 8/20/03).

Gao teach a method of eliciting both a mucosal and systemic (by inducing IgA) immune response in a mammal by administering interleukin-1β via an intra-mucosal route. Gao also teach that the antigen and adjuvant are not conjugated together and that this composition is free of mineral adjuvants,

preservatives, or stabilizers and is in a pharmaceutical composition (Abstract; page 871, column 2). Gao showed that subcutaneous administration of Ig and IL-1β induced strong mucosal as well as systemic antibody response (page 872, top column to page 873 column 2; Tables 1 and 2). Gao do not teach mucosal administration of an antigen together with an adjuvant. Gao also do not teach the use of IL-1α, IL-12, IL-15 or IL-18, the recited dosing range and schedule, or the administration of these interleukins with other cytokines, nor do they teach the recited vehicles, including PBS, or use of this composition in humans.

However, Elson do teach that many pathogens invade or cause disease at mucosal surfaces and that mucosal administration has the distinct advantage of being an easy route of administration as well as inducing both systemic and mucosal immune responses (page 391, column 2, paragraph 2).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the present invention to modify the administration method of Gao by administering the antigen-adjuvant composition intramucosally because Elson teach that this route is an easy route of administration and induces both systemic and mucosal immune responses. It would have also been obvious to the artisan to have adjusted both the dose and administration schedule to maximize the effect of the administered composition. It would have also been obvious to administer this composition to humans since Gao teach that this compsotion was safe and effective in calves. The use of PBS as a vehicle would have also been obvious since this is a safe and widely used vehicle for the administration of compounds. Furthermore, since Gao used IL-1β, it would have also been obvious to have used any interleukins with and without cytokines since it would be expected that, if IL-1β is effective in the method of Gao, then the use of any interleukin, including IL-1α, IL-12, IL-15 and IL-18 would also be effective since the family of compounds and administration technique is the same.

B. Claims 64-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abraham et al. (reference C20 on the IDS dated 8/20/03) in view of Elson et al.

Abraham et al. teach that intranasal administration with a composition comprising bacterial polysaccharide as an antigen and IL-2 as an adjuvant resulted in an increased bacterial-specific pulmonary IgA and pulmonary plasma cells (Figures 1, 3 and 4). Abraham also do not teach the use of IL-1α, IL-12, IL-15 or IL-18, the recited dosing range and schedule, or the administration of these interleukins with other cytokines, nor do they teach the recited vehicles, including PBS, or use of this composition in humans.

It would have also been obvious to the artisan to have adjusted both the dose and administration schedule to maximize the effect of the administered composition. It would have also been obvious to administer this composition to humans since Abraham teach that various similar compositions are safe and effective in vivo (page 3719 right column). Furthermore, since Abraham used IL-2, it would have also been obvious to have used any interleukins with and without cytokines since it would be expected that, if IL-2 is effective in the method of Abraham, then the use of any interleukin, including IL-1α, IL-12, IL-15 and IL-18 would also be effective since the family of compounds and administration technique is the same.

5. Conclusion

A. No claim is allowable.

***Advisory information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
March 15, 2004

ROBERT LANDSMAN
PATENT EXAMINER